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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/595,096	06/15/2000	David J. Diller	1073.060	8927

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HESLIN ROTHENBERG FARLEY & MESITI PC  
5 COLUMBIA CIRCLE  
ALBANY, NY 12203

EXAMINER

SHEINBERG, MONIKA B

ART UNIT	PAPER NUMBER
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1631

DATE MAILED: 12/03/2001

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/595,096

Applicant(s)

DILLER ET AL.

Examiner

Monika B. Sheinberg

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_

***Response to Amendment A***

Applicants' arguments, filed 20 September 2001, have been fully considered by they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being plied to the instant application.

***Information Disclosure Statement***

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the ***first paragraph*** of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 11, and 21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

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had possession of the claimed invention. The specification as pointed to (pages 5 and 6) do not disclose any clear contemplation of not using broken fragments as docking ligands, thus the amendments made to claims 1, 11, and 21 are considered new matter. In addition page 32 of the specification discloses the use of the Monte Carlo search algorithm on large molecules. This search algorithm of the disclosure appears critical or essential to the practice of the invention when practiced on large molecules, but is not enabled by the disclosure. The instant application lacks any amount or direction as to the practice of the Monte Carlo search algorithm. Nowhere in the claims or the specification is there a clear and direct explanation as to how and when the stated method is to be applied in a key step of conformer generation. This critical amount of information pertaining to directing one skilled in the art to perform the practice of the present invention is lacking, thus causing undue experimentation. As essential to the practice of the invention, the Monte Carlo algorithm cannot be referenced to a printed publication by the specification. That which is particular to the practice of the present invention must be selected out the referenced text and included the instant application.

Claims 8, 18, and 28, are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The rejection is maintained and reiterated from the previous office action mailed 16 May 2001. The mode of operation in claim 8 remains not enabled in the instant application. Although applicant amended the claims to contain like variables for the operation of subtraction a vector that holds a value and direction (T), from the now vector "hot spot" of a protein. Yet, the

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product of the vector and matrix remain an unlike term that is not enabled for the operation of subtraction from the vector hot spot. The operation of multiplication an now vector ( $A_j$ ) and a matrix that is defined by coordinates is not enabled. The instant application lacks any amount or direction as to the practice of the mathematical equation of line 4. Nowhere in the claims or the specification is there a clear and direct explanation as to how and when the stated method is to be applied in the step of minimization. As such, claims drawn to the operation of minimization of  $I(R, T)$  remain <sup>non</sup>enabled.

The following is a quotation of the *second paragraph* of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 11, and 21 are rejected due to being vague and indefinite in the method claimed. The body of the claim does not perform that which the preamble sets out to do. Instead the body of the claims set forth a virtual or computer implemented method for docking a ligand to a protein. In addition, the steps of the method recited lacks a final step that actually produces the result of a ligand docked at a protein. For the reason that the claimed method preamble set forth a "test tube" method or non-virtual, placing a grid around a binding site of a protein as recited in claim 5 seems an impossible task. Claims dependent from claims 1, 11 and 21 are also rendered vague and indefinite (claims 2-10, 12-20, and 22-30).

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The amended claim 10 recites the limitation "said simple atom pairwise score" in line 3. There is insufficient antecedent basis for this limitation in the claim. A "simple atom pairwise score" does not have antecedent basis but "an atom pairwise score" does (recited in the amended claim 9, line 5).

Claims 5, 6, 15, 16, 25, and 26 recite the limitation "the binding site" in for example lines 3 and 6 of claim 5; and line 3 of claim 6. There is insufficient antecedent basis for this limitation in the claim. A "binding site image" has antecedent basis but not the binding site alone.

Claim 9, 19, and 29 is rejected due to the lack of clarity in the number of optimization steps. The preamble set forth a method of optimization, yet the body of the claim presents a last step of optimization. It is unclear whether this last step of optimizing each ligand position is a summary step or a further step of optimization upon the steps already recited to be performed for optimizing multiple protein-ligand complex formations. Claims dependent from claim 9, 19, and 29 are also rendered vague and indefinite (claims 10, 20, and 30).

The rejection of claim 8, 18 and 28 is maintained and reiterated from the previous office action mailed 16 May 2001, on lack of clarity as to what the equation provided in line 4 of claim 8 is "minimizing".

In addition, the rejection of claim 8, 18, and 28 is maintained and reiterated from the previous offices action due to the confusion caused by a lack of clearly defined values that are set forth in lines 6-10. The operation of subtracting unlike terms remains even though the atom ( $A_j$ ) has been amended to a vector. The operation of multiplication an now vector ( $A_j$ ) and a matrix that is defined by coordinates is unclear.

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***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 9, 11-17, 19, 21-27, and 29, are rejected under 35 U.S.C. 102(b) based upon anticipation of the invention, by Ho et al. (Pro. of 27<sup>th</sup> Hawaii Int'l Conf. on System Science, 1994).

The rejection is maintained and reiterated from the previous office action mailed 16 May 2001. Applicants argue that Ho et al. teaches a method that uses fragments of chemical compounds while the instant invention uses the “entire” chemical compound. A fragment of a chemical compound still contains the capabilities of providing an effector portion as a whole compositional compound. In addition the claims only state conformational structures, which encompass fragments of compounds. A ligand itself is a generic term, thus a small molecule or a fragment are encompassed by the term “ligand”. The claimed method of docking reads upon initial docking methods as well, or anchor fragments. Thus the argument that Ho et al. does not teach the use of complete ligand structures is moot.

Therefore, the arguments are non-persuasive to overcome the rejection.

Claims 8, 10, 18, 20, 28, and 30 are rejected under 35 U.S.C. 102(b) based upon anticipation of the invention, by Ho et al. (Pro. of 27<sup>th</sup> Hawaii Int'l Conf. on System Science, 1994).

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Ho et al. asserts each component with, for example FOUNDATION or CAVITY, of the instant invention that make up the instant invention as described in the Office Action mailed out 16 May 2001, and above. The methods of Ho et al. are very similar to those of the claimed invention. Due to the same control functions, same structure analysis, same problem solving occurring within the reference, the method steps disclosed in claim 8 (18 and 28) and in claim 10 (20 and 30) would be a logical consolidation of, but not a patentable feature of the instant invention. Whether the product resulting from the process demonstrated in Ho et al. is the same, is not clear, and the Office does not have the facilities to perform such comparative analyses. The court has said: In re Best: "the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Whether the rejection is based on 'inherency' under 35 USC 102, on 'prima facie obviousness' under 35 USC 103, jointly or alternatively, the burden of proof is the same [footnote omitted]." In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977).

No claim is allowed.

### *Inquiries*

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (703) 306-0511. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, can be reached on (703) 308-4028.



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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

November 30, 2001

Monika B. Sheinberg

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*MBS*